REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Claim Amendments

Claim 13 has been amended to limit a "ROCK inhibitor" to the 4 compounds previously described in claim 17, and to delete "Exoenzyme C3". Claim 17 has been cancelled, without prejudice or disclaimer.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 13 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

This rejection is rendered moot in view of the claim amendments, specifically, the incorporation of the limitations of non-rejected claim 17 into claim 13. Withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 13 and 17 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

This rejection is rendered moot in view of the claim amendments, specifically, the deletion of Exoenzyme C3. Withdrawal of this rejection is respectfully requested.

Consideration After Final Rejection

Although this Amendment is presented after final rejection, the Examiner is respectfully requested to enter the amendments and consider the remarks, as they place the application in condition for allowance. Additionally, the scope of amended claim 13 has been previously considered by the Examiner.

Patentability Arguments

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Rejections Under 35 U.S.C. § 103(a)

Hellberg et al. in view of Lehmann et al.

Claim 13 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Hellberg et al. (WO 03/020281) in view of Lehmann et al. (Inactivation of Rho Signaling Pathway Promotes CNS Axon Regeneration).

This rejection is rendered moot in view of the claim amendments, specifically the incorporation of the limitations of non-rejected claim 17 into claim 13. Withdrawal of this rejection is respectfully requested.

Additionally, Applicants wish to clarify a position of the Examiner, which is set forth in this rejection. The Examiner makes the assertion that C3 is a Rho kinase inhibitor. (Please see page 7, line 10 of the Office Action.) Applicants respectfully assert that the assertion that C3 enzyme is a kind of ROCK (Rho kinase) inhibitors is incorrect, since C3 enzyme inactivates Rho protein and does not inhibit ROCK (Rho kinase). This is shown in the Minambres et al. reference, Journal of Cell Science 119 (2), 271-282, which was submitted with the response filed July 16, 2009.

Hellberg et al. in view of Hara et al.

Claims 13 and 17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hellberg et al. (WO 03/020281) in view of Hara et al. (Protein kinase inhibition by fasudil hydrochloride promotes neurological recovery after spinal cord injury in rats).

This rejection is respectfully traversed.

The Examiner takes the position that Hellberg et al. teach the use of compounds that promote neuron regeneration or neurite outgrowth for the treatment of conditions such as dry eye and other conditions related to corneal nerve damage. The Examiner states that the compounds

are neurotrophic factors, and are used to promote neurite outgrowth. The Examiner admits that **Hellberg et al. do not teach the use of Rho kinase inhibitors, such as fasudil hydrochloride**.

The Examiner takes the position that Hara et al. teach that fasudil hydrochloride (HA 1077) can promote neurological recovery after traumatic spinal cord injuries (SCI). The Examiner also asserts that the reference teaches other agents, such as neurotrophic factors known in the art, that improve neurological recovery in SCI.

The Examiner contends that it would have been obvious for one of ordinary skill in the art to use another neurite promoter such as fasudil for corneal injury, as Hellberg et al. teach the use of compounds such as neurotrophic factors to promote neuron regeneration or neurite outgrowth for corneal disorders, and Hara et al. teach that neurotrophic factors and fasudil are both functionally useful (functionally equivalent) for the same condition (neurological recovery for spinal cord injuries).

Applicants respectfully disagree with the Examiner's position.

First, Hara et al. teach that fasudil hydrochloride shows neurological recovery after **spinal cord injury**. Additionally, the reference, which focuses on fasudil hydrochloride, also makes mention of neurotrophic factors as having shown some effect in improving neurological recovery in experimental SCI (spinal cord injury). However, **the reference fails to teach, or even suggest, promotion of corneal neuritogenesis**. Thus, assuming *arguendo* that this reference may be used to demonstrate equivalence in terms of treatment for spinal cord injury, **this *alleged* equivalence does not carry over to the promotion of neuritogenesis of the corneal nerve**.

Second, one of ordinary skill in the art would have had no basis for employing a ROCK inhibitor for promoting corneal neuritogensis, because the presence of ROCK I and ROCK II in the trigeminal nerve (corneal nerve) cell **was found for the first time by the present inventors**, and is demonstrated in Experimental Example 3. (Please see pages 21-23 of the specification.) In addition, the neurite outgrowth promoting effect of the 4 recited ROCK inhibitors is shown in Experimental Example 2. (Please see pages 14-17 of the specification.)

The presence of ROCK I and ROCK II in the trigeminal nerve cell was not known before the filing date of the present application. Thus, contrary to the assertion by the Examiner, one of ordinary skill in the art would not have envisioned that the compounds recited in Applicants'

claim (particular ROCK inhibitors) may be used for promoting neuritogenesis of the corneal nerve (trigeminal nerve).

Third, it is untenable to assume that a compound which is successful in treating **spinal cord injury** may be simply substituted into a method for treating **corneal injury**. Specifically, the method described in the Hara et al. reference involves **intraveneously** administering fasudil hydrochloride, while the method of Hellberg et al. involves the **intraocular** administration of neurotrophic factors. It is unreasonable to assume that a compound which may be intraveneously administered for treatment of spinal cord injuries may be substituted into a composition which is to be introcularly administered for treatment of injury to corneal nerves.

Fourth, absent the use of Applicants' disclosure, one of ordinary skill in the art would not have been motivated to employ fasudil hydrochloride, as taught by Hara et al. as showing some effect in treating spinal cord injury, for promotion of corneal neuritogenesis. As stated by the Supreme Court in KSR International Co. v. Teleflex Inc., "the factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." (See KSR International Co. v. Teleflex Inc., 237 S. Ct. 1727 (U.S. 2007), referring to Graham v. John Deere Co. of Kansas City, 86 S. Ct. 684, which warned against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "guard against slipping into the use of hindsight".

For the reasons set forth above, the invention of claim 13 is clearly patentable over the cited combinations of references. [Claim 17 has been cancelled.]

Double Patenting Rejection

Claim 13 is rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent 7,485,654.

This rejection is rendered moot by the amendments to the claims, specifically the incorporation of the limitations of non-rejected claim 17 into claim 13. Withdrawal of this rejection is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Amendment, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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